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PATENT
Attorney Docket No. **MSU-04769**

#12

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Christoph Benning, *et al.*
Serial No.: 09/709,020 Group No.: 1652
Filed: 11/08/2000 Examiner: Y. Pak
Entitled: **Compositions and Methods For The Synthesis And Subsequent Modification Of Uridine-5'-Diphosphosulfoquinovose (UDP-SQ)**

DECLARATION OF DR. CHRISTOPH H. BENNING PURSUANT TO 37 C.F.R. § 1.132

Assistant Commissioner for Patents
Washington, D.C. 20231

CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8(a)(1)(i)(A)

I hereby certify that this correspondence (along with any referred to as being attached or enclosed) is, on the date shown below, being deposited with the U.S. Postal Service with sufficient postage as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231.

Dated: March 11, 2002 By: Traci E. Light
Traci E. Light

I, Dr. Christoph H. Benning, under penalty of perjury, state that:

1. I am a joint inventor of the subject matter claimed in the above captioned United States Patent Application.

2. I have reviewed the following journal articles:

A. "Essigmann *et al.*, "Prediction of the Active-Site Structure and NAD^+ Binding in SQD1, a Protein Essential for Sulfolipid Biosynthesis in *Arabidopsis*," *Arch. Biochem. & Biophys.*, 369: 30-41 (1999)(hereinafter "the Essigmann paper"); and

B. "Güler *et al.*, A Cyanobacterial Gene, *sqdX*, Required for Biosynthesis of the Sulfolipid Sulfoquinovosyldiacylglycerol," *J. Bacteriol.*, 182(2): 543-45 (2000)(hereinafter "the Güler paper").

3. I am a co-author of the Essigmann. This paper describes experiments conducted to determine the structure of the active site of the SQD1 enzyme protein. The Essigmann paper is completely silent on how the enzyme protein works, whether the enzyme must be an active (*i.e.* functioning) protein, how one would express (*i.e.* recombinantly) and

isolate such an active protein, or how one would assay its activity. Unlike the present invention, the Essigmann paper does not disclose all of the four *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose: active SQD1 enzyme, UDP-glucose, sulfite, and the appropriate buffer conditions. Furthermore, the discussion of a "sulfur donor" is made within the context of a chemical synthesis scheme. The papers cited as references 43 and 44 in support of the discussion of sulfite all refer to chemical synthesis reactions, not enzymatic biosynthesis methods.[1] The Essigmann paper only suggests a model of how a plant may make sulfite. The paper does not disclose that sulfite is "the" sulfur donor in an enzymatic biosynthesis method to produce UDP-sulfoquinovose by using SQD1, UDP-glucose, sulfite, and the appropriate buffer conditions.

4. With respect to Figure 1 of the Essigmann paper (and its corresponding text), the figure is completely silent on the use of a first and second recombinant (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and SQDG. Figure 1 merely depicts a "*model* of the sugar-nucleotide pathway for sulfolipid biosynthesis" without providing direction as to the appropriate buffer conditions, sulfite, and recombinant enzymes required for a biochemical method to produce UDP-sulfoquinovose and SQDG as claimed by the present invention. There is also no suggestion of such an approach in the text of the Essigmann paper.

5. I am a co-author of the Güler paper. This paper describes the disruption and restoration of sulfolipid production in cyanobacteria by removal and replacement of the *sqdX* gene. The reference is completely silent on the use of a first and second recombinant peptide (*i.e.* SQD1 and *sqdX* respectively) in a biochemical method to produce UDP-sulfoquinovose and convert it to SQDG. The reference neither discusses, nor suggests, the *critical* elements of the enzymatic biosynthesis of UDP-sulfoquinovose and its conversion to SQDG: active SQD1 enzyme, UDP-glucose, sulfite (as the sulfur donor), active sqdX (or AtSQDX-1) enzyme, diacylglycerol, and the appropriate buffer conditions.

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[1] Moreover, the paper cited as reference 41 only discusses sugar modifying enzymes in general and mentions UDP-4-keto-5,6-glucoseen (*i.e.* not UDP-SQ or SQDG). Reference 41 is also completely silent with respect to sulfite.

6. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

Dated: 11/8/02

Christoph H. Benning